the weakened heart to resist dilatation, if not already present, to lessen it possibly, or prevent its increase, if it has already developed.

Finally, I would insist that when we consider that apart from rheumatism, syphilis, alcoholism, continued bodily strain, with poor food and hygiene, cardiac dilatation, acute or slowly developed, is mainly occasioned by ignorant, injudicious, careless treatment of the early convalescent period following acute infectious disease, we must recognize the immense importance of my subject to every practitioner of medicine. Inasmuch as I believe cardiac dilatation is a preventable disease in these instances, its importance is only still greater.

NOTE.—Since writing my paper I am delighted to know that by the will of the late W. W. Smith, architect, of New York City, the bequest of nearly $3,000,000 is made to St. Luke's Hospital Corporation, New York City. Mr. Smith stipulates that the money be applied "to the care and relief of needy convalescent patients recovering from acute diseases and surgical operations and from these and other causes requiring care and treatment, not obtainable in their homes, and without regard to religious belief or sex." Noble man, noble gift!

NON-FATAL COMA IN THE COURSE OF DIABETES.[1]

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THE case of diabetes here reported was observed clinically for a period of nine months. The patient developed coma, from which she recovered, and four months later died in hemiplegia. Postmortem examination was made. The opportunity to follow such a sequence of events being comparatively uncommon, the report is thought to be of sufficient interest to add to the records now accumulating with regard to coma in diabetes as well as coma in general.

Report of the Case up to the Development of the Coma (In Brief). A woman, aged forty-eight years, was admitted to the City Hospital, February 27, 1907. Her complaint was nausea. Syphilis had been contracted, but when was doubtful. The patient was of feeble mentality; talkative. There was considerable thirst, large appetite, and other symptoms of diabetes, which seemed to have existed for about two years. There was a moderate degree of general arteriosclerosis. Chart I presents the urinary findings up to the time the coma developed.

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[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1907.

CHART I.—COMA IN COURSE OF DIABETES. RECORD PRIOR TO COMA.

Date.	Amount in c.c.	Specific gravity.	Albumin.	Casts.	Reaction.	Sugar.		Acetone.	Diacetic acid.	Urea in grams:	Symptoms.	Weight in lbs.	Diet.
						Fermentation. Per cent.	Amount in grams.						
Feb. 22	2800	1038	+	+	Acid.	2.5	70	++	0	16.8	Those common to diabetes of about three years' duration. In addition, patient is feeble mentally and has arteriosclerosis. Feb. 13 and Mar. 31, slight incontinence of urine.	—	Restricted. Consisting largely of beef-juice, eggs, and milk.
" 25	1800 +	1030	+	+	"	2.8	—	++	0	15.7		—	
" 27	2400	1037	+	+	"	3.5	84	+++	0	14.7		—	
Mar. 5	2400	1037	+	+	"	3.5	74	++	0	19.2		101·5	
" 7	2203	1030	+	+	"	3.7	82	++	0	22.3		—	
" 10	2460	1027	+	+	"	2.3	56	+	0	21.7		—	
" 13	2650	1032	+	+	"	2.9	77	+	0	15.2		—	
" 19	1400 +	1028	+	+	"	2.6	—	+	0	10.6		102	
" 25	2550	1028	+	+	"	—	—	++	0	18.4		103·5	
Apr. 12	960 +	1030	+	+	Neut.	—	—	—	—	—		—	
" 28	2480	1025	+	+	"	—	—	—	—	22.32		—	

Report of the Coma. For the first two and one-half months after the patient was admitted a detail examination of the urine was recorded (Chart I). This was then discontinued until June 3, when the house physician reported that the patient had recently become irritable, had refused to save the urine, and had considerable ~~diarrhœa, which had resisted ordinary remedies. For several days~~ past (June 3) she had complained of weakness and muscular pain, especially in the back. She frequently fell asleep in her chair. There was some incontinence of urine and feces (diarrhœa) at these times. On the day previous (June 2) she had slept in her chair the greater part of the day, but would arouse as persons approached, and remain awake while they conversed with her. On June 4 the drowsiness markedly increased; she responded only when shaken, and then complained in a heavy manner of general pain, and quickly lapsed into her former conditions. There was incontinence of urine and feces. The breathing was audible, like that of one in deep sleep. It was never labored or irregular, that is, no dyspnœa (Kussmaul) was observed. June 5, the patient could not be aroused. Alkaline treatment was instituted on this date: Milk diet; bicarbonate of sodium, xxx grains (2 grams) by mouth every hour; saline enemas, one pint (500 c.c.) every six hours; hypodermoclysis (saline), one pint (500 c.c.) twice daily. If the urine remained acid to litmus or the patient's condition did not improve, bicarbonate of sodium was to be administered subcutaneously and intravenously. If an alkaline reaction of the urine appeared, the quantity of bicarbonate of sodium was to be reduced. Chart II presents the urinary findings during the coma.

It will be observed in this table that during the coma the specific gravity fell; the volume for twenty-four hours was about the same as that before the coma; the reaction was acid until June 8; the sugar was much reduced; acetone and diacetic acid were present in small quantity and β-oxybutyric acid was absent; ammonia was low; indican was not increased and there was a moderate amount of albumin and occasional casts. With the clearing of the coma the diacetic acid and acetone disappeared (in this order), the amount of sugar and the specific gravity increased. The urine remained acid to phenolphthalin, but on June 8 was alkaline to litmus. This, together with the lessening of the coma, contra-indicated an increase in the amount of alkali to be administered. About 2070 grains (150 grams) had been given in three days, in addition to saline enemas and hypodermoclysis. If an acidosis of any severity were present in this case, it is evident that the amount of alkaline administered was insufficient to counteract it. The alkalizing of the urine, however, indicated that sufficient alkali had been administered to overcome such acidosis as was present. The importance of this, as a diagnostic point, will be referred to again.

CHART II.—COMA IN COURSE OF DIABETES. PERIOD OF COMA

Date.	Amount in c.c.	Specific gravity.	Albumin.	Casts.	Acidity in terms 1/10 Nor. NaHO.	Reaction.	Sugar.			Acetone. Per cent.	Diacetic acid. Per cent.	β-oxybutyric acid.	Indican.	Total grams N. in 24 hours.	Ammon. per cent. of total N.	Total amt. ammon. N in grams in 24 hrs.	Symptoms.	Treatment.	Diet. Total fluids.
							Fermentation. Per cent.	Polariscopic. Per cent.	Amount in grams.										
June 3	1500	1030	+	+	—	Acid	—	—	+	—	—	—	—	—	—	—	Onset of coma: irritability; weakness; muscular pains; asleep in chair most of day; arouses and converses as persons approach; refuses to save urine or obey orders; diarrhœa.	Plan for alkaline treatment: sod. bic., gr. xxx every hour by mouth; saline enemas, Oj every 6 hours; hypodermoclysis, saline 500 c.c. b. d., till urine is alkaline; intrav, and subcut. sod. bic. if condition is worse.	Milk and water 38 ounces.
" 4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	Developing coma: asleep most of the day; responds only when shaken, then lapses into former state; no Kussmaul respiration.		Milk and water 54 ounces.
" 5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	Coma established: cannot be aroused; incontinence of urine, feces; no Kussmaul respiration at any time.	Alkaline treatment begun: sod. bic., gr. xxx every hour by mouth, 23 doses (690 gr.); saline enemas, Oj every 6 hours (2 qts.); hypodermoclysis, saline (500 c.c.).	Milk, 34 oz. Water, 110 oz.
" 6	1680	1030	+	—	—	Acid	—	—	+	+	+	—	—	—	—	—	Coma continues: somewhat less marked; incontinence urine; specimen obtained by catheter.	Sod. bic., gr. xxx every hour by mouth, 23 doses (690 gr.); saline enemas, Oj every 6 hours (2 qts.).	Milk, 38 oz. Water, 30 oz.
" 7	1478	1028	+	+	—	Acid	—	1	14.78	0.00193	0.00048	0	0	—	—	—	Coma lessening: heavy but can be aroused; "sleeps" all day.	2070 gr. sod. bic. by mouth; 6 qts. saline enemas; 500 c.c. saline subcutaneously in 3 days.	Milk, 30 oz. Water, 42 oz.

" 8	1080	1022	+	+	—	Alk.	2.5	—	45.36	+	+	0	—	—	—	—	Coma clearing: sleeping lightly all day.	Sod. bic., gr. xxx by mouth, 3 doses (90 gr.); saline enemas, Oj every 6 hours (2 qts.).	Milk, 52 oz. Water, 40 oz.
" 9	1350	1009	+	+	2.5 c.c.	Alk. lit. acid phen.	0.69	1	13.50	0.0116	0.2209	0	0	6.04	10.6	.041	Coma clearing: brighter but still drowsy.	"	Milk, 18 oz. Water, 66 oz.
" 10	1410	1009	+	+	0.6 c.c.	Alk. lit. acid phen.	0.46	0.52	7.32	0.00348	0	0	0	5.66	8.3	.470	Coma clearing: brighter falls asleep when left alone.	"	Milk, 62 oz. Water, 12 oz.
" 11	1020	1010	++	+	3.0 c.c.	Alk. lit. acid phen.	0	0.08	13.05	0.00464	0	0	0	6.23	13.8	.860	Coma clearing: can be aroused easily.	"	Milk, 72 oz. Water, 2 oz.
" 12	1710	1014	+	+	2.8 c.c.	Alk. lit. acid phen.	0.69	0.06	11.7	0	0	0	0	8.85	14.0	1 22	Disappearance of coma: tried to get out of bed.	"	Milk, 48 oz. Water, 20 oz.
" 13	1800	1009	+	+	1.6 c.c.	Alk. lit. acid phen.	—	0.24	4.46	0	0	0	0	6.67	18.5	1.21	Absence of coma: bright; got out of bed.	Sod. bic., gr. xxx by mouth, 3 doses (90 gr.).	Milk, 61 oz. Water, 14 oz. 2 eggs.
" 14	1833	1015	+	+	1.8 c.c.	Alk. lit. acid phen.	1.8	1.86	32.0	0	0	0	0	16.9	14.5	2.3	Absence of coma: quite rational.	"	Milk, 86 oz. Water, 46 oz. 2 eggs.

+ = present; 0 = absent; — = examination not made.

The blood pressure was as follows: Record of maximum and minimum blood pressure for eight months: February and March, 140 to 220 mm.; April, 130 to 210 mm.; May, 120 to 150 mm.; June (period of coma), (Chart III); July, 90 to 150 mm.; August, 150 to 220 mm.; September, 150 to 210 mm.; October and November (period of hemiplegia, prior to death), 160 to 240 mm., 200 constant (Chart IV).

Report Subsequent to the Coma. From June 15 to October 24, 1907, the patient showed no evidence of coma. She remained well and active, assisting about the ward; her mental condition was such as had been noted on admission. On October 24, 1907, she again lapsed into a drowsy condition. Acetone, which had been present all along, disappeared from the urine; diacetic acid did not appear. The amount of sugar remained unchanged. Albumin and casts continued to appear as on previous examinations, with some increase in the albumin. Albuminuric retinitis was found. The blood pressure, at this time, will be seen in Chart IV.

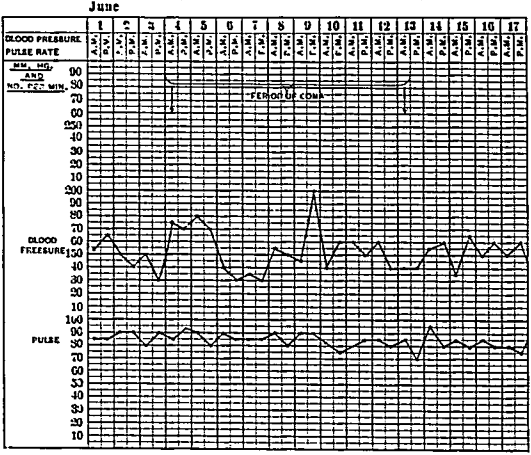

CHART III.—Blood pressure chart during June, period of coma. Compare this chart with that for October and November (Chart IV).

On October 25, 1907, definite hemiplegia developed and continued until death occurred, November 20, 1907.

Autopsy by Dr. Horst Oertel (Report in Brief). Female body, about forty-eight years of age, 170 cm. long; long, slender frame, fair amount of emaciation; skin, pale, clear; pupils: left, oval, medium size; right, dilated, round; there is a small arcus senilis.

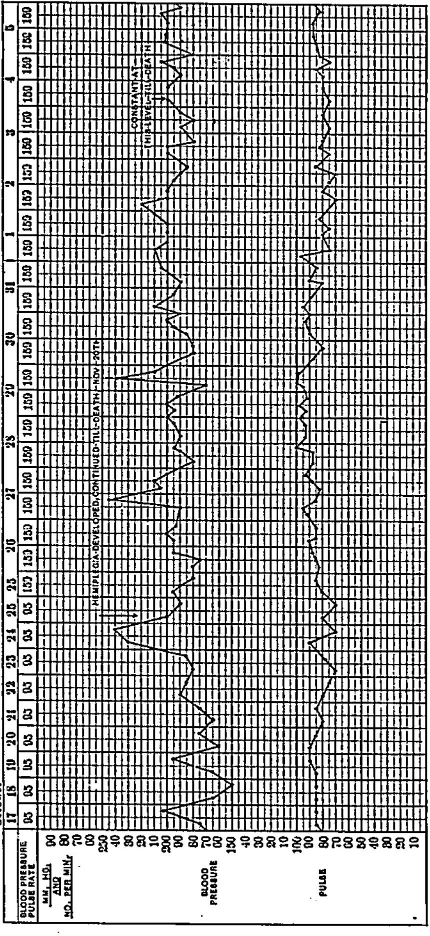

CHART IV.—Blood pressure for October and November; period of hemiplegia, just prior to death. Compare blood-pressure chart of this date with that of June, period of coma (Chart III).

On opening the thorax the left plural cavity is dry and free from adhesions, the right plural cavity is dry and contains a few adhesions over the apex and over the lower lobe in the axilla.

Heart. Mitral valves: Posterior valve cusp shrunken; anterior contains large, irregular patches, which are yellowish and have wavy raised edges. The aortic valves are wrinkled and slightly stiffened at their bases. The aortic above contains numerous gamboge-yellow raised patches. The coronaries are small, tortuous, and contain numerous deep, yellow, raised patches. The heart muscle on section is brownish with yellowish mottled areas; the muscle bundles are not distinct; in place there are small white areas.

Left Lung. The lung is small, its anterior portions crepitant, its posterior portions bluish, wet, œdematous. There are a few subpleural calcified tubercles, which are surrounded by black anthracotic areas. Upper lobe is crepitant, dry. The pleura at apex is negative. The lower lobe is firmer, wet, and exudes a small amount of frothy serum. The smaller bronchi are slightly reddened. *Right Lung.* The right lung is larger; the upper lobe contains a few puckered pleural thickenings, and on section it is reddish and exudes on pressure frothy serum. Some of the smaller bronchi exude purulent material, and the lobe contains scattered areas which are firm, but from which cut section sinks. The middle lobe is crepitant, emphysematous. The lower lobe is dark red, and contains scattered areas of consolidation, and exudes on pressure frothy serum. The smaller bronchi, especially those of the lower lobe, are bathed in mucopurlent material.

Spleen. Negative.

Left Kidney. Weight, 185 grams. The kidney is quite large, surrounded by a small amount of perinephric fat; it measures 13 x 7 x 4 cm. The capsule strips with some difficulty, leaving a finely, and in places roughly, granular surface. The lobulations are fairly well marked, and in places contain whitish puckered scars. On section the cortex has an average thickness of 10 mm.; it is yellowish and greasy; the Malpighian bodies not at all distinct. The medulla is reddish in color and the line of demarcation well preserved.

Right Kidney. Weight, 180 grams. Same as left.

Duodenum. Small, with well-marked rugæ. The papilla is prominent and exudes fluid bile on pressure. Common, cystic, and hepatic ducts free.

Liver. Weight, 1500 grams. Its surface is smooth, and contains mottled yellowish areas. On section it has a somewhat greasy surface. The centres of the lobules appear dark red in color. The periphery of the lobules is light yellow.

Pancreas. On removing the pancreas, which is rather small, the tail of the organ not reaching the hilum of the spleen, the weight is found to be 100 grams. The organ measures 17 cm. from head to tail. Its middle part is 5 cm. broad and 3 cm. thick. It is surrounded by very little fat. On cut section, firm; the lobules are irregular in size, pinkish, and separated widely by bands which have a butter-like consistency. The pancreatic duct is apparently surrounded by a large amount of connective tissue. The splenic artery shows moderate atheroma. The pancreatic, common, and hepatic ducts and the gall-bladder are free from stones. Microscopic section shows interstitial and marked interacinar pancreatitis; sclerosis of and diminution in the number of islands; great destruction of pancreatic lobules, bringing islands into clumps.

Brain. The brain is small, there being apparently atrophy of both frontal lobes. The vessels at the base of the brain are small, tortuous, and filled with atheromatous plaques. On opening these vessels the lumen gaps and the walls are clotted. On section of the brain a small area of softening is found in the right internal capsule along the motor tract. This area is elongated, being about 5 mm. by 1 cm. It is entirely limited to the motor tract. There is also considerable fluid in both lateral ventricles. The brain substance around this area is very soft. In the right pons is also a small area of softening about 4 mm. in diameter, well localized. Along the motor tracts the spinal cord grossly shows no area of degeneration. The posterior spinal vessels, however, are thickened and tortuous.

ETIOLOGY OF THE COMA. 1. *Acidosis or Acid Intoxication.* At the annual meeting of the Association of American Physicians held in 1907 Dr. Folin[2] presented a review of the work done on acid intoxication, and Dr. Joslin,[3] at the same meeting, presented a similar paper on acidosis. From these two papers it appears that, though for the last fifty years much work has been done in Germany and in this country on the high ammonia content and organic acids in diabetes, there is as yet no clear knowledge of either the source of these acids or the part they play in the graver stages of this disease. The chemical features, however, of these conditions are now well established, and from the record here given it can be stated definitely that neither existed in this case. The ammonia remained unusually low throughout the coma, and the diacetic acid was present in small quantity only; β-oxybutyric acid did not appear at any time (Charts I and II). That it would be incorrect to assume the absence of acidosis upon this latter negative finding alone has been pointed out by several authors. Dr. Lusk, with Dr. Mendel, reported a case in which there was absolute intolerance for carbohydrates, and yet for three weeks no β-oxybutyric acid could be detected in the urine, and there was a maximum output of but 0.8 gram. of acetone daily. But this, together with the low ammonia, small total output of urine in twenty-four hours, and prompt alkalizing of the urine with small amounts of alkali (see discussion of treatment below), indicates the absence of acidosis or acid intoxication in this case.

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[2] Trans. Assoc. Amer. Phys., 1907, xxii, 256.

[3] Ibid., p. 246.

2. *Uremia.* The urine showed nothing in regard to nephritis, which does not occur in many cases of diabetes. Albumin was present throughout. The great increase in the characteristic casts described by Kulz[4] did not occur at the time of the coma, though casts were at all times present. The most significant finding was the blood pressure (Charts III and IV). The blood pressure ran moderately low during the coma, but in the final attack, which was associated with hemiplegia, the pressure rose and remained uniformly high until death. Albuminuric retinitis showed definitely that nephritis was present. Autopsy showed a chronic diffuse parenchymatous nephritis, which, although indicated by the urine and retinitis, could not, from any clinical manifestation, be held accountable for the coma. Beyond the blood pressure changes and the absence of increase in albumin, we must consider that there were no clinical signs by which uremia as a cause of the coma could be included or excluded.

3. *Brain Softening.* This patient showed from the beginning mental weakness. There was a history of syphilis and evidences of general arteriosclerosis. This evidence was in hand at the time of the onset of the coma. Cases in literature are not lacking[5] to show the frequent association between diabetes and encephalomalacia. Four weeks before death hemiplegia developed, and definite evidence of this condition was found postmortem. At the time of coma, however, we had not these facts, and the stupor was different in no way clinically from graver forms in diabetes. The mental weakness, the incontinence of urine and feces, together with mild diabetes and absence of signs of acid intoxication, were important facts pointing to the central nervous system. The subsequent hemiplegia was very significant. There is no explanation as to how coma, in such brain conditions, is produced.

4. *Disturbed Proteid Metabolism.* Although nitrogen partition was made in this case, it seems inadvisable to attempt conclusions from one case. This portion of the record, therefore, is omitted.

ALKALINE TREATMENT. This, while of no value therapeutically in the present case, proved to be so diagnostically. It will be remembered that treatment, as recommended by Stadelmann and followed by Naunyn and Magnus Levy, required 100 grams of bicarbonate of sodium a day. As high as 80 grams have been injected intravenously, the reaction of the urine being the guide to the quantity to be administered. In the case here reported 150 grams by the mouth in three days was sufficient to alkalize the urine. This was in itself evidence of either the absence of acid formation or, if present, in quantity insufficient to account for such grave clinical manifestations as appeared.

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[4] Domansky and Reimannn, Ztschr. f. Heilk., 1901, and Herrick, AMER. JOUR. MED. SCI., 1900, vol. cxx.

[5] Frerich, Ogle, Dreyfus, etc., cited by Naunyn.

CONCLUSIONS. From the foregoing evidences the, case seems to have been one of syphilitic arteriosclerosis (history of syphilis, presence of arterial thickening, arcus senilus, and aortic cardiac sclerosis), with involvement of the pancreas, kidney, and brain. The sclerotic changes in the pancreas (interacinar pancreatitis) led to the diabetes, those in the kidney (chronic parenchymatous nephritis) to the chronic nephritis (albuminuria, casts, and albuminuric retinitis), and those in the brain to the softening with hemiplegia, to the feeble mentality, and possibly to the coma.

At the bedside, when the coma appeared, the syphilitic history, the arteriosclerosis, the enfeebled mentality, the mild grade of diabetes, the absence of any increase in the diacetic acid, the non-appearance of β-oxybutyric acid, the low ammonia, the small quantity of alkali required to alkalize the urine, the absence of any increase in total quantity of urine in twenty-four hours, seemed to be clinical features differentiating this coma from the graver forms. The subsequent hemiplegia was very significant. The low blood pressure and absence of any increase in albumin and casts were suggestive, but not positive signs by which uremia could be excluded. The urinary findings and the small amount of alkali required to alkalize the urine seem in themselves important guides in diagnosis and safeguards against false conclusions with regard to the part played by the alkaline treatment.

The only coma in diabetes clinically defined is the dyspnœic type, and the only coma chemically defined is that due to acidosis and acid intoxication. The diagnosis of these conditions, as a rule, offers no great difficulty. It is the atypical group or that due to complications which occurs more frequently and which presents the real diagnostic and prognostic problem to the clinician. The nephritis and brain condition are most important in the consideration of the coma, but in the absence of any clear knowledge of how coma is produced in uremia or brain softening, the mere statement of their presence is not sufficient to exclude other factors resulting from disturbed metabolism (proteid for example) which subsequent investigation may disclose.

The discussion of the case with nine months' clinical record, and, finally, the postmortem findings before one is very different from the problem offered the clinician at the bedside at the onset of the coma. At that time it was impossible to say that fatal coma was not developing. I believe two important findings at that time justified one in assuming that the coma was of mild type, namely, the character of the urine and the amount of alkali required to neutralize the urine. In forty-eight hours from the onset of the coma these features manifested themselves. While no explanation of the coma appears in the record, these clinical findings may prove to be features differentiating the comparatively common non-fatal coma in diabetes (due possibly to complication or some yet unexplained metabolic disturbance) from the rapidly fatal coma in this disease.

The laboratory examinations were done in the Strecker Laboratory under Dr. Oertel and in the Cornell Clinical Laboratory under Dr. Hastings. I wish to thank Drs. Woodruff and Groeschel, house physicians, for their interest and care in preparing the records.

Dr. Joslin kindly reviewed the records with regard to the question of acidosis, or acid intoxication, and his opinion is expressed in the following letter:

"In my opinion the case . . . illustrates coma simulating the coma of acid intoxication, and yet certainly has absolutely no connection with that form. It is essential for physicians to remember this possibility, and not to treat all cases of coma in diabetes as if due to acid intoxication. The case is further valuable because so often in the past cases of coma in diabetes have been said to occur without proving the acidosis. This case was carefully studied, acidosis eliminated, and coma proved to be of another type.

"The case was evidently mild diabetes, because the carbohydrate balance was pretty certainly, from the records given, positive rather than negative. For example, the greatest quantity of sugar was 84 grams on February 27, and yet evidently considerable milk was used at that time, and the diet probably contained more than this amount of carbohydrates. Further, the case was evidently mild, because there was no diacetic acid in the urine during February, March, April, and only a very small quantity in June. Diacetic acid constitutes only about 10 per cent. of the total acidosis, and acetone constitutes only about 10 per cent. of the combined acetone and diacetic acid. Consequently we are absolutely certain that the acidosis was insignificant.

"For the above reasons it is not necessary to know more details of the urine during the coma, because the analyses before and after settle the severity of the case. There are a few additional factors which help to exclude the acidosis: First, the fact that the urine became alkaline on June 8, during the coma, while the patient was taking an insignificant quantity of alkali, *e. g.*, 2 grams hourly. Second, the total quantity of urine at no time exceeded 2000 c.c. No case of diabetic acidosis, to my knowledge, has been reported without Nature making an effort, by the passage of large quantities of liquid, to wash out acids from the body. Third, the increase in the percentage of ammonia was very slight, and the total quantity far too low to enable one to claim acidosis."